188 History of Genitourinary Disease

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Urinary Tract Infection

Definition

A urinary tract infection may involve the urinary tract at any level, including renal parenchyma, renal pelvis, ureters, bladder, and urethra. Infections above the ureteropelvic junction (UPJ) are termed *upper tract;* infections below the UPJ are termed *lower tract.* Infection of the renal parenchyma is termed *pyelonephritis.*

Technique

Most patients who have had significant urinary tract infection in the past will be aware of the diagnosis. The questioner should begin with general queries such as, Have you ever had any kidney trouble or kidney problems? Have you ever been told of having a kidney, bladder, or other urinary tract infection? If the patient is unable to provide details spontaneously, mention features of urinary tract infection and inquire whether the patient has experienced them. Ask whether the patient had voiding symptoms (frequency, urgency, dysuria) alone or whether fever, chills, nausea, vomiting, general malaise, and flank pain were present instead or in addition to the voiding symptoms. The former group of symptoms is characteristic of lower tract infection, the latter of upper tract infection. Next ask about the medical evaluation of past infections. Such inquiries may provide valuable information about the severity and type of disease. Ask whether intravenous pyelography (IVP), ultrasonography, cystoscopy, or voiding cystourethrography were performed. The procedures may be briefly described to prompt the patient to recall what was done. An unsophisticated patient may not remember an IVP as such, but will recall an x-ray procedure during which a dye that caused flushing was injected into a vein. Few patients forget cystoscopy.

Inquire about associated risk factors for urinary tract infections. Some, such as chronic indwelling catheter drainage of the bladder due to paraplegia from trauma or from spina bifida, will be self-evident. Others, such as neurogenic bladder from diabetic autonomic neuropathy, bladder outlet obstruction due to urethral valves, prostatism, urethral stricture, analgesic abuse neuropathy with papillary necrosis, or ureteral stricture from recurrent renal colic, can be inferred from proper questioning.

The treatment of pyelonephritis or complicated urinary tract infection usually requires hospitalization and parenteral antibiotic therapy. Cystitis is typically treated with oral, outpatient therapy. Recurrent urinary tract infections may be treated with chronic suppressive regimens. Thus, questions relating to the type and duration of treatment also clarify the nature of a previous urinary tract infection. Determine whether the infection was an isolated event or whether it was recurrent. If recurrent, ask whether chronic suppressive antibiotic therapy was prescribed and whether urine cultures were obtained during asymptomatic intervals.

Basic Science

Infection of the urinary tract occurs by two principal routes. Bacteremia can result in seeding of the renal parenchyma. This is particularly likely in individuals with preexisting renal disease of another type, including chronic glomerulonephritis, diabetic nephropathy, or chronic interstitial nephritis. Infection may also occur by an ascending route, with spread from the urethra to the bladder and upper tracts. The latter is more common in females because of the much shorter distance from the urethral meatus to the bladder and because of the proximity of the meatus to the vagina and rectum. Manipulation of the urethral meatus can introduce bacteria into the bladder; urine cultures obtained from women after coitus show a high rate of positivity. Manipulation during urologic procedures such as cystoscopy or catheterization also predispose to lower tract infection and to ascending infections. The prevalence of bacterial colonization of the urinary tract of patients with bladder catheters that have been in place more than 72 hours is virtually 100%. Urologic manipulation of an obstructed or partially obstructed urinary tract is especially likely to induce severe infection.

Clinical Significance

The severity of urinary tract infection is variable. Cystitis is an important cause of discomfort and inconvenience but is not life threatening and seldom leads to permanent damage of the urinary tract. Treatment is aimed at alleviation of symptoms. When recurrent cystitis is a problem, urinary suppression with chronic antibiotic therapy may be indicated. Pyelonephritis can lead to permanent renal scarring and dysfunction or to septicemia and death. These complications are especially likely to result when obstruction and pyohydronephrosis are present. Of uncertain significance is so-called asymptomatic bacteriuria, positive urine cultures without symptoms. It was formerly believed that this was a manifestation of chronic pyelonephritis and could lead to

renal failure. In the absence of underlying structural renal disease, however, asymptomatic bacteriuria is probably not a cause of progressive renal damage. It is quite difficult to separate asymptomatic colonization of the upper tract from that of the lower tract. Techniques such as bladder washout or ureteral catheterization are definitive but invasive. Testing voided bacteria for coating by antibodies (often present with tissue infection) is noninvasive but neither adequately sensitive nor specific.

It is important to know whether a urinary tract infection is associated with a significant anatomic lesion. Treatment of a remediable lesion may prevent further episodes of infection and damage to the urinary tract from obstruction caused by the lesion. Cystitis is common in young women and probably does not warrant an anatomic investigation. Evaluation of repeated episodes has a low yield but may be indicated. Lower tract infection is rare in males with normal urinary tracts. Like upper tract infections in any patient, lower tract infection in males should be investigated with appropriate anatomic studies.

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Past History of Stones

Definition

In a patient with a past history of nephrolithiasis, stones may have been single or multiple, unilateral or bilateral. They may have been discovered as an incidental, asymptomatic finding on x-ray, have passed spontaneously, or required urologic intervention for removal.

Technique

Because renal colic is one of the most severe forms of pain, few patients will have difficulty recalling a full-blown episode of colic. If there is doubt, effort should be made to differentiate between renal colic and the forms of abdominal or back pain with which it may occasionally be confused. Except with simultaneous passage of bilateral stones, renal colic is unilateral. It typically begins with an aching pain in the region of the costovertebral angle that later becomes lancinating and excruciating. As the stone descends in the ureter, so does the pain, moving inferiorly and anteriorly to the lower quadrant of the affected side and finally radiating into the scrotum and penis or labia. The pain will persist at a given spot until the stone moves farther along the ureter. Pain is commonly associated with nausea and diaphoresis. Although some residual aching may persist, significant relief of the pain occurs with passage of the stone beyond the ureterovesical junction into the bladder.

Ask the patient about the character and duration of the pain. Ask whether there has been just one episode of colic or several, and whether the episodes were unilateral or bilateral. Ask whether the stones passed spontaneously or whether urologic manipulation was required. If necessary, was the manipulation from below, involving cystoscopy and ureteral catheterization with a snare, or ureteroscopy with lithotripsy. Ask whether an open ureterolithotomy or pyelolithotomy was necessary. Ask whether there was associated infection.

Ask whether a cause of the nephrolithiasis was determined. Many patients will know whether the retrieved stone was analyzed, whether it contained calcium, or whether it was an "infection stone." The metabolic evaluation of recurrent nephrolithiasis requires extensive testing. Patients will not know the details but should have some recollection about whether or not they were put through the relatively complicated work-up required. Typically, patients are asked to follow a calcium-restricted diet temporarily and to collect 24-hour urine specimens. Ask whether this was done. Ask also about any treatment measures instituted since the stone passage. Such regimens vary. Some patients will be asked only to increase their fluid intake. Others will be given more specific instructions such as drinking at least 2 liters per day, drinking two glasses of water upon retiring and again in the middle of the night when they arise to void, or measuring 24-hour output periodically to verify that the daily urine flow is above 2 liters. Inquire also about specially prescribed diets, including low calcium, oxalate, or purine diets. Ask also about prescribed medications such as thiazide diuretics or oral phosphate therapy. Finally, ask about risk factors for stone disease such as a positive family history, inflammatory bowel disease, purine or oxalate gluttony, myeloproliferative disorders, or gout. Vitamin preparations containing vitamin D and absorbable antacids containing calcium (e.g., Tums or other calcium carbonate preparations) also pose a risk for stone formation. Recall that large amounts of oxalate are contained in spinach, rhubarb, beet greens, some kinds of nuts, chocolate, and improperly brewed tea. Ingestion of large quantities of vitamin C may also lead to an increase in oxalate excretion, although not all authorities agree.

Basic Science

Most stones contain calcium in varying combination with oxalate, phosphate (apatite), or magnesium and ammonium (struvite). Others are formed of uric acid or cystine. Stones form because of supersaturation of the urine with one of these substrates. Supersaturation occurs if daily excretion is abnormally high, but may also exist at normal daily excretion rates if urinary pH shifts or there is a lack of urinary solubilizing agents.

Calcium is present in approximately 90% of all stones. Roughly 80% are the oxalate or apatite salts. Frequently

there is no definable urinary abnormality, but documentable causes include excess calcium excretion, excess oxalate excretion, and the chronically alkaline pH and urinary citrate deficiency seen with renal tubular acidosis. Ten percent of stones contain apatite associated with magnesium ammonium phosphate, or struvite. These stones result from infection with urea-splitting bacteria such as proteus. The resulting high urinary pH favors precipitation of struvite, forming typical staghorn calculi with infection. Calcium nephrolithiasis is associated with hypercalciuria in 30 to 60% of cases. Hypercalciuria may occur because of the increased filtered load of calcium that results from the hypercalcemia that may accompany conditions such as hyperparathyroidism or sarcoidosis. More commonly, it occurs without hypercalcemia, as in absorptive hypercalciuria or renal hypercalciuria. In the former, intestinal calcium absorption is increased above normal, and the excess calcium appears in the urine. In some of these cases, 1,25-dihydroxyvitamin D levels are elevated; stimulation of intestinal calcium absorption by vitamin D is the presumed mechanism of the hyperabsorptive state. Patients with renal hypercalciuria have defective renal tubular calcium reabsorption, leading to excessive excretion. These two disorders may be distinguished by comparing urinary calcium excretion in the fasting state to postprandial excretion. Both groups of patients are hypercalciuric after calcium meals, but hypercalciuria persists during fasting in the renal but not the absorptive hypercalciurics.

Because calcium oxalate is poorly soluble, excessive oxalate excretion readily leads to calcium oxalate nephrolithiasis. This occurs in primary hyperoxaluria, an autosomal recessive disorder characterized by a defect in the glyoxylate pathway that leads to excessive oxalate production. Hyperoxaluria can also result from ingestion of oxalate-rich foods (see above), or from increased intestinal absorption of oxalate. The latter typically results from inflammatory bowel disease involving the terminal ileum. The resultant fat malabsorption diminishes the availability of calcium to complex with oxalate in the gut and allows the presentation of oxalate to the colon in a more absorbable form.

The non-calcium-containing stones include cystine and uric acid. Cystine stones occur with cystinuria, an autosomal recessive defect in proximal tubule reabsorption of dibasic amino acids. Cystinuria is accompanied by increased excretion of lysine, ornithine, and arginine.

Even with normal uric acid production, urine can be supersaturated with respect to uric acid. Urate stones may thus occur in normouricosuric individuals. More commonly, urate nephrolithiasis is associated with hyperproduction and hyperexcretion of urate due to a myeloproliferative disorder or purine gluttony.

Clinical Significance

Stones are likely to recur. Many types of stone disease are treatable. Thus a history of stone passage in the past should prompt the physician to determine whether the etiology has been sought and specific therapy prescribed. If not, such an evaluation should be undertaken.

Stones are causes of significant morbidity. Renal colic is agonizing; no patient wants a recurrence. The repeated episodes of colic cause a significant loss of productive time. In addition, blockage of the ureter predisposes to urinary tract infection. Stone impaction or the procedures required to alleviate it may be complicated by ureteral stricture that can later produce obstructive uropathy. As it is impossible to eradicate infection from a stone matrix, recurrent or persistent stones serve as a nidus for infection. In the case of struvite stones, the infection itself favors stone formation, initiating a cycle that can lead to formation of staghorn calculi, severe renal cortical scarring, and marked loss of renal function with all of its sequelae.

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Family History of Genitourinary Disease

Definition

A number of renal diseases are hereditary, so a positive family history may be significant.

Technique

The interviewer should begin with general questions and follow with specific questions if the history is positive. Lead off by inquiring whether anyone in the family has had kidney disease or kidney trouble. If so, determine whether the disorder involved infection, stone passage, kidney failure, hypertension, proteinuria, or hematuria. Patients ordinarily will not have knowledge about the specific diagnosis of glomerulonephritis but will often have been told about having excess protein in the urine. They may recognize edema if a relative has had problems with swelling or if the relative is taking diuretics, or "water pills." Ask if any affected relatives have received dialysis (i.e., kidney machine treatments) or kidney transplants. Polycystic renal disease is a common, autosomal dominant inherited disorder that leads to end-stage renal disease. In affected families, several members who have reached middle age are likely to be receiving dialysis treatments. Members of previous generations, persons who developed end-stage renal disease before the ready availability of dialysis, will have died of renal failure. Asymptomatic children of the affected family members may have been screened for evidence of the disease. Thus, members of such families may be quite sophisticated

in their knowledge of this disorder. It is usually possible and always appropriate to construct a family tree indicating which family members are affected. In other heritable disorders, such as Alport's syndrome or benign familial hematuria, the severity of the disease in affected individuals is much more variable. In these families, it will be more difficult to establish a pedigree.

Although many renal disorders are heritable, most are not. A positive family history does not always imply an increased risk of renal disease in the patient.

Basic Science

There are a number of types of familial renal disease. Several forms of cystic diseases are heritable. Adult polycystic disease is an autosomal dominant disorder with 100% penetrance. Although it may not become manifest until the seventh or eighth decade, it usually presents in the third or fourth decade with hypertension, hematuria, infection, or pain due to bleeding into a cyst; end-stage renal disease develops over the ensuing ten years. Childhood polycystic disease is an autosomal recessive disorder with features similar to the adult form except that end-stage renal disease is attained within the first decade. The nephronopthisis–cystic renal medulla complex is characterized by corticomedullary or medullary cysts, interstitial fibrosis, and progressive renal failure. Salt wasting may be an important clinical feature. Although 15 to 20% of cases are sporadic, 50% of cases, the juvenile form, are characterized by autosomal recessive inheritance. An additional 15% with renal-retinal dysplasia have associated retinal disease. Twenty percent of cases present in early adulthood with the adult variant, a form with autosomal dominant inheritance.

Several forms of heritable renal disease are associated with deafness. Alport's syndrome is usually inherited as an

Table 188.1
Selected Heritable Renal Disorders[a]

Disorder	Mode of inheritance	Features
	CYSTIC DISORDERS	
Adult polycystic	Autosomal dominant	Cysts distributed throughout kidney; CRF; adult onset
Juvenile polycystic	Autosomal recessive	Similar features to adult form; CRF in first decade
Juvenile nephronopthisis—cystic medullary disease	Autosomal recessive (15 to 20% of cases sporadic)	Medullary cysts; CRF; adult, juvenile, and renal–retinal variants
	DISORDERS WITH PREDOMINANTLY GLOMERULAR INVOLVEMENT	
Alport's syndrome (hereditary nephritis)	Autosomal dominant; sex-linked or preferential segregation in some families	Proteinuria, hematuria, CRF; sensorineural deafness; ocular abnormalities
Muckle-Wells syndrome	Autosomal dominant	Amyloidosis, CRF; deafness
Chacot-Marie-Tooth disease	Autosomal recessive	Proteinuria, nephrotic syndrome; peripheral neuropathy; deafness
Benign familial hematuria	Autosomal dominant or recessive	Recurrent or persistent hematuria
IgA nephropathy	Familial form of uncertain mode of inheritance; usually sporadic	Recurrent hematuria
Fabry's disease	X-linked	Proteinuria, hematuria, CRF; hemizygotic females variably affected
Familial Mediterranean fever	Autosomal recessive	Amyloidosis, CRF; serositis, arthritis, fever
Congenital nephrotic syndrome	Autosomal recessive	Nephrotic syndrome, CRF
	DISORDERS PRESENTING WITH RENAL TUBULAR FUNCTION ABNORMALITIES	
RTA, type I (distal)[b]	Autosomal dominant	Metabolic acidosis, nephrolithiasis; growth retardation in juvenile-onset forms
RTA, type II (proximal)[c]	Autosomal recessive	Usually occurs with Fanconi's syndrome; growth retardation, rickets
Cystinosis	Autosomal recessive	RTA, Fanconi's syndrome, growth retardation; proteinuria, nephrotic syndrome, CRF
Cystinuria	Autosomal recessive	Cystine nephrolithiasis
Primary hyperoxaluria	Autosomal recessive	Oxalate nephrolithiasis
Nephrogenic diabetes insipidus	X-linked	Polyuria, polydipsia, hypertonic dehydration
Calcium nephrolithiasis	Uncertain	History of nephrolithiasis obtainable in up to 25% of first-degree relatives of stone formers

[a]This table is not meant to be a comprehensive listing of all heritable renal disorders. Multisystem disorders in which the renal manifestation is unlikely to be the presenting feature as well as a number of more rare disorders have been omitted.

[b]Type I RTA may occur alone or as a feature of the autosomal dominant disorders hereditary elliptocytosis and Marfan's syndrome, the usually dominantly inherited Ehlers-Danlos syndrome, or with the recessive disorders, including sickle cell disease, Wilson's disease, and erythrocyte carbonic anhydrase B deficiency.

[c]Type II RTA may occur alone or as a feature of the autosomal recessive disorders cystinosis, tyrosinosis, hereditary fructose intolerance, galactosemia, pyruvate carboxylase deficiency, and glucose-6-phosphatase deficiency and the X-linked disorder, Lowe's syndrome.

CRF = chronic renal failure; RTA = renal tubular acidosis.

autosomal dominant disorder, although in some kindreds male-to-male transmission has not occurred, making preferential segregation or sex linkage the likely form of transmission. Clinical features of the disorder include microscopic or gross hematuria, proteinuria, renal failure, sensorineural deafness, and ophthalmic abnormalities. Although males and females are equally likely to be affected, the renal disease is of greater severity and the likelihood of progression to end-stage renal failure is greater in males. Charcot-Marie-Tooth disease is an autosomal recessive disorder characterized by proteinuria and nephrotic syndrome and peripheral neuropathy. Muckle-Wells syndrome is characterized by autosomal dominant inheritance of deafness and amyloidosis with renal involvement.

Another important heritable renal disorder is renal tubular acidosis (RTA). Type 1, or distal, RTA is frequently associated with hypercalciuria and/or nephrolithiasis. Type 2, or proximal RTA, is commonly associated with the Fanconi syndrome, a constellation of proximal tubular disorders including aminoaciduria, glycosuria, hyperuricosuria, and phosphate wasting that may lead to renal rickets. Either proximal or distal RTA can cause growth retardation if it presents in childhood. Inheritance of these disorders in isolated form is usually autosomal dominant. They may also occur in association with more generalized, autosomal recessive disorders.

Table 188.1 lists the heritable diseases mentioned above and some of the other, less common inherited renal disorders.

Clinical Significance

Knowledge of the family history of renal disease is an important piece of diagnostic information. If the family history is well established, the need for extensive diagnostic evaluation or invasive procedures is curtailed. A renal biopsy will probably not be necessary to explain the hematuria in a member of a family known to carry Alport's syndrome. If more "objective" documentation of carriage of a defective gene is deemed necessary, an abnormal audiogram might well substitute for renal biopsy.

Conversely, a lack of family history can also be important diagnostically. The renal ultrasound or intravenous pyelogram of an individual with several simple renal cysts may resemble that of an individual with early polycystic kidney disease. The lack of a family history of polycystic kidney disease will strongly favor the former diagnosis.

In addition, information about family history is essential for genetic counseling and to decide about appropriateness of screening of potentially affected parents, siblings, or children.

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